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PD-1 Blockade Enhances Therapeutic Vaccine Potential in a Chronic SIV/Macaque Model

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Background: Limitations to achieving a complete HIV-1 cure include failure to remove latent reservoirs, CD8 T cell dysfunction due to immune exhaustion, and restricted homing of anti-viral CD8+ T cells in lymphoid tissue where most reservoirs persist, even under anti-retroviral therapy (ART). These findings warrant the development of strategies that can simultaneously improve virus-specific T cell functions, enhance cytolytic CD8 T cell localization to lymphoid structures, reduce reservoir burden under ART, and sustain these responses in the absence of ART. The combined action may enable an effective viral control in the absence of ART potentially leading to a complete remission.

Methods: Three groups of rhesus macaques (RMs) were infected with SIVmac239 intrarectally and ART was initiated at ~10 weeks post infection. Two groups were subsequently immunized with two DNA-SIV239/MVA-SIV239 prime/boost vaccines. The third group served as the control group. Both vaccinated groups also received ectopic applications of the imiquimod (a TLR7 agonist) as a potential immune adjuvant/latency reversal agent. The Vaccine plus PD-1 group received anti-PD-1 antibody prior to ART initiation and concomitant with the DNA priming. All vaccinations were carried out under complete viral suppression by ART. RMs were followed for 26 weeks post-analytical treatment interruption and tracked for the viral rebound, development of AIDS, and survival. Key parameters such as T cell response, reservoirs, and lymph node localization of cytolytic CD8 T cells were interrogated longitudinally at key time points of the study.

Results: We show that CD40L adjuvated DNA/MVA vaccine induced highly functional SIV-specific CD4+ and CD8+ T cell responses in blood, gut, and lymph nodes (LN) under anti-retroviral therapy. Combining PD-1 blockade with vaccine markedly increased the frequency of granzyme B+ perforin+ CD8+ T cells in blood and LN, enhanced their localization to B-cell follicles, and reduced viral reservoir. Upon ART interruption, combination therapy showed marked preservation of the granzyme B+ CD8+ T cells in the T cell zone and BCF regions of LN, maintained high SIV antigen-recognition breadth, showed notable control of reemerging viremia, and significantly improved survival, but not vaccine alone or control animals.

Conclusions: Our findings reveal that PD-1 blockade enhances the therapeutic benefits of vaccination by improving and sustaining the function and localization of vaccine-induced CD8 T cells to BCF and decreasing viral reservoirs.
Cardiometabolic health and birth outcomes among pregnant women living with and without HIV in South Africa

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Background: HIV and antiretroviral therapy (ART) influence cardiometabolic health, but there are few data on the cardiometabolic impact of HIV and ART on birth outcomes.

Methods: We enrolled women living with HIV (WLHIV) and HIV-infected women at 24-28 weeks’ gestation. WLHIV were on pre or post conception efavirenz- or dolutegravir-based ART. At enrollment, women underwent a fasted 2-hour oral glucose tolerance test for gestational diabetes (GDM), diagnosed via WHO guidelines. Blood pressure and anthropometry was assessed by trained research staff. Hypertension was defined as ≥130/80 mmHg. Self-reported pre-pregnancy weight was used to estimate pre-pregnancy body mass index (BMI; obesity = pre-pregnancy BMI ≥ 30). Birth outcomes were assessed via medical records.

Results: Among 315 women (HIV-uninfected = 149, WLHIV=166 (n=58 dolutegravir, n=102 efavirenz), the median age at first antenatal visit was 30 (IQR 25,34), gestational age 17 weeks (IQR 12, 21), and 53% of women were obese pre-pregnancy (HIV-uninfected 56% vs WLHIV 49%). Overall 11% of women had hypertension and 4% had GDM. Adjusted for age and pre-pregnancy BMI, HIV did not increase the risk of hypertension (RR 0.79, 95% CI 0.41, 1.49) and marginally increased risk for GDM (RR 3.33, 95% CI 0.71, 15.51) although estimates were imprecise. Among 182 deliveries to date, women with hypertension had a higher proportion of small-for-gestational age infants (birthweight <10th percentile; 30% vs 11%, p-value 0.02). Women with GDM had a lower proportion of large for gestational age infants (>90th percentile, 0% vs 16%, p-value 0.24), but experienced more emergency cesareans (57% vs 20%, p-value 0.14) and delivered earlier (median 37 weeks’ gestation vs 39 weeks). There were no important differences in birthweight or preterm birth between women with hypertension or GDM during pregnancy and those without.

Conclusions: In this cohort of pregnant HIV-uninfected and WLHIV, over 50% were obese pre-pregnancy. HIV was not associated with hypertension in mid-pregnancy, but marginally increased GDM risk. Women with hypertension were more likely to have a small-for-gestational age infant, while women with GDM had high level of emergency cesarean sections. Addressing cardiometabolic health in pregnancy may improve some birth outcomes among WLHIV and HIV-uninfected women.
"I do know [about PrEP] is from How to Get Away with Murder": Black Women's Perceptions of PrEP

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Background: In the Atlanta metropolitan statistical area (MSA), African American women are 15 times more likely to acquire HIV than white women. Yet, they account for less than 2% of PrEP users nationally.

Methods: The current study presents the data collected from 21 Black cisgender women during 6 focus group discussions. Most participants were not married (71%) and had private insurance (57%). Focus groups were conducted via Zoom and by the project director and trained research assistants using a vignette about a Black woman who was interested in PrEP as a discussion prompt. Groups were audio-recorded, transcribed, and analyzed using rapid qualitative analysis.

Results: The focus group discussion highlighted several areas of consideration. PrEP Knowledge. PrEP awareness was high among participants, however, most women expressed uncertainty about whether PrEP was appropriate for women. Seeking Health Information. Women reported that others may seek information about PrEP due to perceived HIV risk; wanting to understand if it was for women, and wanting to know more about PrEP side effects and interactions with other medications. Women highlighted the importance of marketing that reflects that PrEP is for Black women. PrEP Point of Care. Some women reported that they would like to receive PrEP from their SRH provider because of their established relationship -with the level of comfort depending on the gender, race, and age of the provider. Other women had concerns about stigma and costs and reported that women would rather go to a non-stigmatizing setting that provided financial assistance for medical care. PrEP disclosure. Most women reported that women would not disclose their PrEP use to others if they were to initiate PrEP. PrEP Adherence. Lastly, participants reported that adherence to PrEP could be challenging, and most, although not all, women reported that they would prefer an injectable form of PrEP instead of oral PrEP.

Conclusions: Black cisgender women have not been engaged in the PrEP roll-out in the Atlanta MSA. Future work is needed to highlight the appropriateness of PrEP for this population, support PrEP initiation and adherence, and build capacity for providers to offer PrEP to their Black cisgender women patients.
Perceptions of South Carolina Pharmacists Toward Providing HIV Pre-Exposure Prophylaxis

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Background: HIV pre-exposure prophylaxis (PrEP) is underutilized in South Carolina (SC) with the Centers for Disease Control estimating only 6.5% of eligible persons aged 16 years being prescribed it in 2017. To expand access to PrEP for at-risk individuals, pharmacists are well-positioned within the community, including rural settings where access to PrEP is limited, to use their medication and counseling expertise. Whether pharmacists in SC are ready to prescribe PrEP remains unknown.

Methods: A 43-question survey was created in collaboration with the Duke Initiative on Survey Methodology to assess SC pharmacists’ comfort, knowledge, and readiness to provide PrEP. Utilizing the University of South Carolina College of Pharmacy listserv, 2680 pharmacists received the online survey via Qualtrics (Provo, UT). Data collection occurred between September and October 2020.

Results: A total of 150 pharmacists responded with 11% practicing in rural locales. The majority of respondents were 73% White, 83% non-Hispanic, and 62% female. The range in practice was diverse: retail 25%, hospital-based 22%, independent 17%, community 13%, specialty 6%, and academic 3%. Mean years of experience was 17 (range 1-50). Only 53% of respondents viewed HIV as common in their community. Almost all respondents were aware of PrEP (93%) and 41% had dispensed the medication before. Respondents viewed PrEP as both effective (98%) and beneficial (74%) for patients. Many respondents reported being ready (61%) and willing (86%) to prescribe PrEP if allowed and described pharmacies as an appropriate location to prescribe PrEP (72%). However, there were differing opinions among pharmacists on who should be offered PrEP and some pharmacists requested additional training due to lack of awareness of PrEP management.

Conclusions: The vast majority of SC pharmacists surveyed considered PrEP to be effective and beneficial for their patients and are willing to prescribe this therapy if authorized. Many felt that pharmacies are an appropriate location to prescribe PrEP, but lack a complete understanding of required protocols to manage these patients. Further investigation into facilitators and barriers of pharmacy-driven PrEP are needed to enhance utilization within communities.
Implications of Belief in Undetectable=Untransmittable for HIV Transmission Worry, Sexual Openness, and Sexual Wellbeing Among MSM with Undetectable HIV

Sarah Calabrese, PhD

Background: Undetectable=Untransmittable (U=U) is a powerful message that could enhance the lives of many people with HIV by correcting widespread misconceptions about transmission risk and alleviating associated worry. This study examined the association of U=U belief with HIV worry, sexual openness, and sexual wellbeing among men who have sex with men (MSM) with undetectable HIV. Additionally, we examined HIV worry as a mediator of associations between U=U belief and sexual outcomes.

Methods: In 2019-2020, we recruited MSM ages 18+ for a US-based, online survey study about HIV viral suppression and prevention (N=457); the current analysis was restricted to participants with HIV reporting an undetectable viral load (n=96). The survey assessed awareness of U=U; belief in U=U (i.e., belief that someone with a sustained undetectable viral load has zero risk of sexually transmitting HIV); worry about sexually transmitting HIV to HIV-negative sexual partners; openness to having sex with HIV-negative men (using/not using PrEP and with/without a condom); and sexual wellbeing (sexual anxiety, esteem, and satisfaction). Linear regression and bootstrapped mediation analyses were adjusted for race, income, and recency of HIV diagnosis.

Results: Participants were 20-78 years old (M[SD]=45[12.81]). Most were White (66%) and identified as gay (95%). Nearly all had heard of U=U (99%), but only 68% believed it. Despite their undetectable status, 39% of participants expressed worry about transmitting HIV to partners. U=U belief was associated with significantly lower HIV worry (β=-.22, p=.03). In (unmediated) linear regression models, U=U belief was not significantly associated with sexual outcomes (all p>.05). However, mediation analyses revealed three significant indirect pathways through HIV worry: Participants reporting U=U belief were less worried about HIV transmission, which was associated with more openness to condomless sex with an HIV-negative partner not taking PrEP (bootstrapped indirect effect [BIF]=.23, SE=.12, 95%CI[.01,.50], p<.05), sexual esteem (BIF=.16, SE=.10, 95%CI[.00,.38], p<.05), and sexual satisfaction (BIF=.17, SE=.10, 95%CI[.01,.41], p<.05).

Conclusions: Belief in U=U was directly associated with less HIV worry and indirectly associated with more sexual openness, esteem, and satisfaction. Interventions that increase understanding and perceived credibility of U=U may be psychologically and sexually empowering for people with HIV.
Iron, folic acid, and multiple micronutrient supplementation strategies during pregnancy and adverse birth outcomes in Botswana

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**Background:** The risk of adverse birth outcomes is especially high in Sub-Saharan Africa, particularly among women living with HIV. Antenatal multiple micronutrient supplementation (MMS) with iron, folic acid, and other micronutrients may improve birth outcomes but is not currently universally recommended by World Health Organization.

**Methods:** We performed pregnancy surveillance for adverse birth outcomes at government maternities in Botswana following routine initiation of four supplementation strategies among women presenting before 24 weeks gestation: folic acid only, iron only, iron and folic acid (IFAS), and MMS. We estimated risk differences (RDs) overall, by HIV status, and in other key subgroups, adjusting for demographic and clinical factors.

**Results:** Among 96,341 eligible women (22.5% with HIV), those who took iron only (n=36,334) or folic acid only (n=1,133) rather than IFAS (n=23,101) had higher risks of stillbirth, preterm and very preterm delivery, low and very low birthweight, and neonatal death (RDs [95% CIs] for iron only versus IFAS ranging from 0.22% [0.04%, 0.40%] for neonatal death to 2.39% [1.78%, 3.00%] for preterm delivery; RDs [95% CIs] for folic acid only versus IFAS ranging from 0.77% [-0.80%, 2.34%] for neonatal death to 5.75% [1.38%, 10.13%] for preterm delivery), with greater difference among women with HIV and those ≥35 years. Compared with IFAS, women who took MMS (n=31,588) had lower risks of preterm and very preterm delivery, and low and very low birthweight (RDs [95% CIs] ranging from -0.50% [-0.77%, -0.23%] for very preterm delivery to -1.06% [-1.69%, -0.42%] for preterm delivery).

**Conclusions:** Our findings support IFAS as an essential part of antenatal care to reduce adverse birth outcomes, with greater benefits among women with HIV and women age ≥35 years. Our findings also highlight that MMS may be superior to IFAS in terms of the risk of preterm delivery, very preterm delivery, low birthweight, and very low birthweight. Programs may consider MMS in pregnancy to maximally reduce adverse birth outcomes.
CSF Biomarkers of Inflammation and Immune Activation Associated with Neurocognitive Impairment among Latinos Living with HIV

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**Background:** Latinos are at higher risk for HIV-associated neurocognitive impairment (NCI) compared to non-Latino Whites. Neuronflammation is often increased in HIV and among racial/ethnic minorities, and has been linked to NCI. We aimed to examine the association between markers of inflammation in the CSF and NCI among diverse persons with HIV (PWH).

**Methods:** We performed a retrospective cross-sectional analysis of 363 PWH (126 Latinos, 237 Whites; overall cohort: age: M=42.5, SD=11.0, 88% male, 51.5% AIDS history; 64% on antiretroviral therapy [ART]). Neurocognitive function was measured via a comprehensive neurocognitive battery, and NCI was defined using demographically-adjusted global deficit scores. Participants underwent a lumbar puncture for collection of CSF biomarkers (interleukin-6, interferon-γ-inducible protein-10 [IP-10], soluble CD14 [sCD14], neurofilament light chain [NFL]). Covariates included demographic, HIV disease, medical, psychiatric and substance use characteristics.

**Results:** Latinos had significantly higher NFL levels than Whites (p=0.02, Cohen’s d=0.56), with no other significant CSF biomarker differences. A logistic regression model on NCI showed a marginally significant CSF IL-6 by ethnicity interaction, such that higher CSF IL-6 increased concurrent risk for NCI in Latinos (OR=4.6, CI=0.9-24.1) but not in Whites (OR=0.68, CI=0.2-1.9). In the entire cohort, higher sCD14 was associated with increased risk for NCI when controlling for significant covariates (OR=2.9, CI=1.1-7.7), and IP-10 was marginally so (OR=1.9, CI=0.9-3.8).

**Conclusions:** CSF neurodegenerative and inflammatory biomarkers are important prognostic indicators of NCI and may vary by ethnicity. Future studies might examine sociocultural factors that lead to increased inflammation in the CSF in diverse samples of PWH.
Association of Human Immunodeficiency Virus Infection with Outcomes Among Adults Hospitalized with COVID-19

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**Background:** Whether HIV is associated with worse outcomes among hospitalized individuals living with HIV is unknown. Therefore, the objective of this study was to evaluate the association of HIV infection with outcomes among people hospitalized with COVID-19.

**Methods:** Design: Prospectively-planned analysis of the American Heart Association’s COVID-19 Cardiovascular Disease Registry. Setting: 107 academic and community hospitals in the United States from March through December 2020. Participants: Consecutive sample of 21,528 adults hospitalized with COVID-19 at participating hospitals. Main Outcome and Measure: Primary outcome was pre-defined as in-hospital mortality. We used hierarchical mixed effects models to assess the association of HIV with in-hospital mortality accounting for patient demographics, comorbidities and clustering by hospital. Secondary outcomes included major adverse cardiac events (MACE), severity of illness, and length of stay (LOS).

**Results:** The registry included 220 people living with HIV (PLWH). PLWH were younger and more likely to be male, Non-Hispanic Black, on Medicaid, and active tobacco users. Of the study population, 36 PLWH (16.4%) died compared with 3,290 (15.4%) without HIV (Risk ratio 1.06; 95% CI 0.79-1.43; p=0.71). After adjustment for age, sex, race, and insurance, HIV was not associated with in-hospital mortality (aOR 1.13; 95% CI 0.77-1.6; p=0.54) with no change in effect after adding body mass index and comorbidities (aOR 1.15; 95% CI 0.78-1.70; p=0.48). HIV was not associated with MACE (aOR 0.99; 95% CI 0.69-1.44, p=0.91), COVID severity (aOR 0.96; 95% CI 0.62-1.50; p=0.86), or LOS (aOR 1.03; 95% CI 0.76-1.66; p=0.21).

**Conclusions:** In the largest study of PLWH hospitalized with COVID-19 in the United States to date, we did not find significant associations between HIV and adverse outcomes including in-hospital mortality, MACE, or severity of illness.
Scratching below the Surface: An Exploration of Challenges faced by Ethnic Minority Women living in the United States (US) At-Risk for Falling out of HIV Care, and Opportunities for Intervention Design

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Background: Patient-level (e.g., psychiatric, substance use) and structural-level (e.g. discrimination/stigma) factors are barriers to achieving optimal health among racial/ethnic minorities with HIV. We examined relationships between subjective and objective measures of adherence and known barriers/facilitators to HIV care among racial/ethnic minority women. Findings will inform equitable, culturally- and linguistically-competent, technology-based interventions designed for women at-risk of falling out of care.

Methods: Cross-sectional data were collected from a convenience sample of African-American, Haitian-American and Hispanic-American women receiving HIV care in Southern Florida, an HIV/AIDS epicenter. Women were surveyed regarding anti-retroviral (ARV) adherence (rating, days taken), medical mistrust (mistrust; GBMM), depressive symptomology (depression; PHQ-9), HIV-related stigma (stigma; HSS), and resiliency (CD-RISC25). Recent HIV viral load (VL) was extracted from the electronic medical record (EMR). Data (N=50) were analyzed by racial/ethnic group and preferred language—a proxy for acculturation linked to health literacy, risk behaviors and patient-provider relationship. Parametric and non-parametric descriptives (proportions, Chi-square, medians [M]), bivariate and post-hoc analyses (Spearman coefficient [R]; Kruskal-Wallis plus Dwass-Steel-Critchlow-Fligner [KW]) tested relationships across and within groups (SAS Studio 9.4).

Results: Significant relationships were found between both objective and subjective assessments of adherence and stigma, depression, resiliency and medical mistrust—across and within linguistic and racial/ethnic groups. Linguistic Group Comparisons: 37% of participants had a recent mental health/psychiatric condition—English-speakers significantly more than others; Spanish-speakers had the lowest proportion (p<0.05). 14% overall had a recent history of drug use—most commonly amongst English-speakers. Creole-speakers had the lowest rate of VL suppression (67%); the highest (92%) occurred amongst the Spanish-speakers. English-speakers self-reported the lowest ARV adherence. Within linguistic group, Creole-speakers “Always” taking ARV endorsed lower mistrust (KW; p<0.03). Ethnic Group Comparisons: Haitian-American women endorsed the highest level of stigma—African-Americans, the lowest (M; p<0.05). Depression correlated positively to stigma (R=0.053; p<0.001) and negatively to resiliency (R=-0.486; p<0.001). Higher depression (M; p<0.05) correlated to VL non-suppression. Amongst Hispanic-Americans, higher stigma correlated to VL non-suppression (M; p<0.05); amongst African-Americans, lower resilience correlated to VL suppression (M; p<0.05).
Conclusions: Findings underscore the importance of understanding the nuanced differences by both racial/ethnic and linguistic group, when designing interventions to improve adherence to HIV care and treatment.
Variation in Statin Prescription among Veterans with HIV and Known Atherosclerotic Cardiovascular Disease

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Background: People with HIV have increased atherosclerotic cardiovascular disease (ASCVD) risk, worse outcomes following incident ASCVD, and experience gaps in cardiovascular care, highlighting the need to improve delivery of preventive therapies in this population. In this study, we sought to identify patient-level correlates and inter-facility variation in statin prescription among Veterans with HIV and known ASCVD.

Methods: Veterans with an ASCVD diagnosis who received HIV care across 130 VA medical centers were studied for the years 2018-2019. Cross-sectional correlates of any statin prescription assessed via VA electronic health record were investigated using two-level hierarchical multivariate logistic regression. We included individual-level variables and facility-level characteristics as fixed-effects in the model, while the individual VA facilities were retained as random-effects. We calculated median odds ratios (MORs) to estimate inter-facility variation in statin prescription.

Results: Veterans with HIV and known ASCVD (N=9608, mean age 64.3 ± 8.9 years, 97% male, 48% Black) were included in the analysis. Only 67% of the participants were prescribed any statin. Substantially higher statin prescription rates were associated with diabetes (OR = 2.3, 95% confidence interval [CI], 2.0-2.6), hypertension (OR = 2.3, 95% CI, 2.1-2.5), history of coronary revascularization (OR = 4.0, CI, 3.2-5.0), CD4 count ≥200 cells/μL (OR = 1.8, CI, 1.5-2.1), and receiving antiretroviral therapy (OR = 3.0, CI, 2.7-3.4). Blacks (OR = 0.7, CI, 0.6-0.9) and those with history of illicit substance use (OR=0.7, CI, 0.6-0.9) were less likely to be prescribed statins. There was significant variation in statin prescription across VA facilities (10th, 90th centile: 55%, 78%) that was not explained by patient- and facility-level characteristics, with an estimated 20% difference in statin prescription for two clinically similar individuals treated at two comparable facilities (MOR = 1.21, 95% CI, 1.18-1.24). Adjusted MORs were 1.32 for Blacks versus 1.14 for White Veterans (p<0.01) indicating greater variation among facilities (in addition to lower statin prescribing practice) for Blacks.

Conclusions: In an analysis of large-scale VA data, we found suboptimal statin prescription and significant interfacility variation in statin prescription among Veterans with HIV and known ASCVD, particularly those who are Black.
Increased Pericardial Fat Deposition is Associated with Subcutaneous Adipose Tissue Inflammation in People with HIV

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**Background:** Redistribution of fat from subcutaneous adipose tissue (SAT) to the pericardium, abdominal viscera, and skeletal muscle is associated with cardiometabolic disease in people with HIV (PWH). SAT inflammation in PWH persists despite plasma viral suppression on antiretroviral therapy (ART) and adipose tissue function. Prior studies by our group found differences in SAT lipid handling gene expression that were associated with hepatic steatosis in PWH. Here, we identify SAT immune-related genes associated with ectopic fat deposition in PWH on long-term ART.

**Methods:** Ninety-two PWH with controlled viremia underwent abdominal SAT lipoaspirations and computed tomography (CT) imaging. SAT gene expression was measured using a Nanostring panel of 255 immune-related genes. Associations between gene expression and CT measurements of the size and attenuation (density) of metabolically relevant ectopic fat depots were assessed using multivariable linear regression and network analysis.

**Results:** Higher pericardial fat volume (PFV) was associated with higher visceral adipose tissue (VAT) volume and lower visceral fat attenuation and liver attenuation. It was not associated with SAT volume or skeletal muscle attenuation. Hierarchical clustering identified a distinct subset of macrophage-related SAT genes associated with increased lipid deposition in several fat depots.

**Conclusions:** Differences in the expression of macrophage-related genes in SAT is associated with metabolically unhealthy deposition of ectopic lipids in the pericardium and visceral adipose tissue compartments. These findings suggest that persistent SAT inflammation despite plasma viral suppression promotes redistribution of lipid storage to ectopic areas. Further studies will assess the host, virus, and treatment factors shaping the SAT immune environment, and whether reducing SAT inflammation may be a strategy to improve hepatic steatosis.
The HIV and STI syndemic following mass scale-up of combination HIV interventions in Uganda: a population-based study

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**Background:** Rollout of combination HIV interventions (CHIs) has led to significant declines in HIV incidence in sub-Saharan Africa; however, the impact of CHIs on the African STI epidemic is unknown.

**Methods:** We measured prevalence of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), *Trichomonas vaginalis* (TV), syphilis, and herpes simplex virus type 2 (HSV-2) among inland agrarian and Lake Victoria fishing populations in southern Uganda following scale-up of antiretroviral therapy (ART) and voluntary medical male circumcision (VMMC). Data were collected among consenting adults, aged 18-49, in the Rakai Community Cohort Study between May and October 2019. CT and NG testing was conducted using nucleic acid amplification testing (Abbott RealTime CT/NG assay). Point-of-care testing was done for TV (OSOM Trichomonas) and syphilis (SDBioline), with subsequent laboratory confirmation of syphilis titers using a rapid plasma regain (RPR) test (Cypress Diagnostics). Participants were classified as having active syphilis infection if their RPR titers were ≥1:8. HSV-2 testing was performed with Kalon HSV-2 IgG ELISA.

**Results:** There were 1,825 participants (n=906 fishing), including 965 women (53%), of whom 9% (n=107) were pregnant. HIV prevalence was 12 and 40% and viral load suppression 91 and 90% among inland and fishing populations, respectively. Overall, there was 6.7% prevalence of NG (n=122), 9.8% CT (n=177), and 11% TV (n=196). In the fishing population, syphilis reactivity was 24% (n=219), with 9.4% (n=85) of the population having titers indicative of active syphilis infection, including 17% (n=26) of HIV-seropositive men. HSV-2 antibodies were detected in 43 and 64% of inland and fishing populations, respectively. While prevalence of at least one STI (NG, TV, CT, or active syphilis) was 1.56 fold higher among HIV-positive versus HIV-negative persons (36 vs 23%; 95%CI: 1.33-1.82), there were no differences in STI prevalence by ART (Prevalence risk ratio [PRR]=1.08;95%CI: 0.75-1.55) or VMMC status (PRR=0.97;95%CI:0.76-1.26). HIV-positive pregnant women were 56% more likely (95%CI:1.34-1.82) to have an STI compared to HIV negative pregnant women.

**Conclusions:** Despite high coverage of CHIs, STI burden remains extremely high in Uganda, particularly among HIV-positive persons. There is an urgent need to integrate STI diagnostic testing and treatment with HIV services in African settings.
COVID-19 vaccination intent among people living with HIV in a high HIV prevalence community

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**Background:** People living with HIV (PLWH) may have a poorer prognosis with COVID-19 infection and are an important population for COVID-19 vaccination. We assessed the willingness and reasons for COVID-19 vaccine acceptance or hesitancy among PLWH in South Africa.

**Methods:** We conducted telephone interviews with a randomly selected subset of participants enrolled in a prospective observational cohort study evaluating a decentralized antiretroviral therapy (ART) delivery program in South Africa. Questions assessed intent to accept a future COVID-19 vaccine, concerns regarding COVID-19 vaccination, and overall vaccine confidence. Interviews were conducted between September 2020 and January 2021. We evaluated participant demographics, sources of COVID-19 information, stigma and medical mistrust, uptake of nonpharmaceutical interventions, and socioeconomic impacts of the COVID-19 pandemic as potential covariates of vaccination intent.

**Results:** We completed interviews with 213 participants; 72% were female with median age 35y. Among the participants, 121 (57%) intended to accept vaccination, with an additional 46 (22%) unsure and 45 (21%) stating they did not intend to be vaccinated. Fear of side effects, reported by 42 (20%), was the most common concern about COVID-19 vaccination. Older age was associated with intention to be vaccinated (aOR 1.75 for every 10-year increase in age, 95% CI 1.10-2.78, p=0.02), while higher medical mistrust related to COVID-19 (aOR 0.21, 95% CI 0.093-0.45, p<0.001) and use of social media for COVID-19 information (aOR 0.30, 95% CI 0.11-0.84, p=0.02) were associated with lower intention to accept vaccination.

**Conclusions:** In this cohort of PLWH in South Africa, over half intended to accept COVID-19 vaccination, though a substantial proportion remained unsure or did not intend to be vaccinated. Public health messaging should emphasize the safety and efficacy of COVID-19 vaccination and address misinformation and medical mistrust among PLWH. Ongoing efforts to ensure access to COVID-19 vaccines for vulnerable populations are crucial.
Transcriptome signature of HIV Latency: Single-Cell Analysis

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Background: Heterogeneity of HIV-infected cell populations and bystander cells is a poorly investigated phenomenon. Novel single-cell RNAseq/Antibody-seq approaches provide an excellent opportunity to elucidate cell divergence during the HIV life cycle.

Methods: We identified and evaluated the gene expression signatures in primary T-cells with latent HIV status, we implemented high-throughput methods for single-cell transcriptome analysis. We used the QUECEL HIV latency/reactivation model, which closely mimics viral lifecycle in HIV-positive patients.

Results: We defined the transcriptome signatures in various sub-populations of primary T-cells infected with HIV, as well as in uninfected bystander populations. Based on the unsupervised clustering of single cell transcriptomes, cells with latent HIV can be divided into three sub-populations: 1) infected cells spontaneously entering latency as early as day 4 after the infection (markers genes: APOBEC3 deaminases, p53 and DNA repair pathway genes); 2) cells driven into latency using a cocktail of cytokines (marker genes represent Interferon-α (IFNA) and Interferon-γ (IFNG) pathways, as well as TNF family members, IL7R, IL32 and allograft rejection-specific genes); 3) TCR-reactivated cells that are lagging in a latent state (marker genes also belong to APOBEC3, IFNA and IFNG pathways). Interestingly, while few cytotoxic T-lymphocytes (CTL) and Natural Killer (NK) cells were detected in the original uninfected T-cell population, we detected a significant elevation in the expression of CTL and NK markers in sub-population 3, i.e., cells retaining the latent transcriptome signature after HIV reactivation. These markers included granzymes, GNLY genes of the CCL cytokine family, as well as IFNG transcripts. We detected significant negative correlations between HIV expression and MYC pathway, genes encoding cell cycle related targets of E2F transcription factors, mTORC1 pathway and DNA repair. Overall, our analysis elucidated multiple pathways that independently contribute to the latency signature of HIV-infected cells (IFNG/IFNA, APOBEC3, p53). Reactivation of latent HIV resulted in highly heterogenous population of lymphoid cells ranging from CTL/NK-like cells to memory T-cells with highly variable levels HIV expression.

Conclusions: Retroviral infection in combination with various regiments of cytokine treatment results in complex differentiation of a homogenous naïve T-cell population. The emergent phenotypes include HIV-negative or HIV-low NK/CTL-like cells, expressing Granzymes A/B, GNLY and IFNG.
Exploring the consequences of HIV/SIV infection in heart

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Third Coast CFAR

Background: Despite the progress with antiretrovirals, people with HIV are about two more times likely to develop heart disease. Numerous studies have demonstrated that chronic inflammation and immune cell activation are elevated in HIV individuals even with efficient elimination of viremia by successful ART.

Methods: Immuno-PET/CT was used to gain three-dimensional insight into viral dissemination in the whole animal. To validate PET/CT data and identify individual infected cells we performed immunofluorescent staining using variety of SIV specific antibodies against Env (KK41/KK42), Gag (Ag3.0) and viral core (KC57). To evaluate the SIV target cell populations in the heart and to phenotype infected cells, tissue sections were stained using antibodies against CD4 (HIV receptor), CCR5 (co-receptor), CD3 (T cells), CD68 (macrophages/dendritic cells) and Tryptase/CD117 (mast cells).

Results: Immuno-PET/CT revealed the presence of virally infected cells in the female reproductive tissue and gastrointestinal tissues, therefore confirming the results from our previous studies where reporter viruses were used to study virus dissemination. Additionally, we detected the virus in a previously unsuspected organ- heart. The levels of virus were impacted by the administration of antiretroviral therapy; we observed a steady decrease in the number of infected cells with continuation of ART. Our studies also suggest that heart may be one of the main organs where virus rebounds after the cessation of 6-month course of ART, further implying the importance of this organ in HIV infection. The phenotyping analysis of the infected cells revealed dramatic differences in infected cell distribution and phenotype between the "rebound" and chronically infected animals. In chronic animals we routinely find large foci of infected cells that include T cells, macrophages, dendritic cells and mast cells. On the other hand, the infected cells in the "rebound" animals are very sparse and appear as isolated events; all infected cells identified to date in these animals are mast cells.

Conclusions: The work described herein demonstrated the presence of SIV infection in rhesus macaque heart and suggests that mast cells may be important virus reservoir in this organ. The future studies will address the impact of infection on local tissue inflammation and activation.
Cellular pathways and virus-host interactions essential for the emergence of HIV from latency

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**Background:** The switch between HIV latency and productive transcription is regulated by an autoregulatory feedback mechanism initiated by the viral trans-activator Tat, which functions to recruit the host transcription elongation factor P-TEFb to proviral HIV. A heterodimeric complex of CDK9 and one of three cyclin T subunits, P-TEFb is expressed at vanishingly low levels in resting memory CD4+ T cells and cellular mechanisms controlling its availability are central to regulation of the emergence of HIV from latency.

**Methods:** Using a well-characterized primary T-cell model of HIV latency alongside healthy donor memory CD4+ T cells, we characterized specific T-cell receptor (TCR) signaling pathways that regulate the generation of transcriptionally active P-TEFb, defined as the coordinate expression of cyclin T1 and phospho-Ser175 CDK9.

**Results:** Protein kinase C (PKC) agonists, such as ingenol and prostratin, stimulated active P-TEFb expression and reactivated latent HIV with minimal cytotoxicity, even in the absence of intracellular calcium mobilization with an ionophore. Unexpectedly, inhibition-based experiments demonstrated that PKC agonists and TCR-mobilized diacylglycerol signal through MAP kinases ERK1/2 rather than through PKC to effect the reactivation of both P-TEFb and latent HIV. Single-cell and bulk RNA-seq analyses revealed that of the four known isoforms of the Ras guanine nucleotide exchange factor RasGRP, RasGRP1 is by far the predominantly expressed diacylglycerol-dependent isoform in CD4+ T cells. RasGRP1 should therefore mediate the activation of ERK1/2 via Ras-Raf signaling upon TCR co-stimulation or PKC agonist challenge. Combined inhibition of the PI3K-mTORC2-AKT-mTORC1 pathway and the ERK1/2 activator MEK prior to TCR co-stimulation abrogated active P-TEFb expression and substantially suppressed latent HIV reactivation.

**Conclusions:** Therefore, contrary to prevailing models, the coordinate reactivation of P-TEFb and latent HIV in primary T cells following either TCR co-stimulation or PKC agonist challenge is independent of PKC but rather involves two complementary signaling arms of the TCR cascade namely, RasGRP1-Ras-Raf-MEK-ERK1/2 and PI3K-mTORC2-AKT-mTORC1.
Short-term binge drinking, marijuana, and recreational drug use trajectories in a prospective cohort of people living with HIV at the start of COVID-19 mitigation efforts in the United States

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**Background:** At the start of the COVID-19 pandemic, HIV experts suggested that an increase in mental health diagnoses and substance use among people living with HIV (PLHIV) may be an unintended consequence of COVID-19 mitigation efforts (e.g., limiting social contact). We evaluated short-term trajectories in binge drinking, marijuana, and recreational drug use in a prospective cohort of PLHIV.

**Methods:** Data (N = 2,121 PLHIV) consist of survey responses on substance use behaviors from two pre-COVID-19 (October 2018-September 2019) and one COVID-19-era (April 2020-September 2020) timepoints within the MACS/WIHS Combined Cohort Study (MWCCS). We conducted group-based trajectory models, triangulated with generalized linear mixed models, to assess changes in binge drinking, daily marijuana use, and recreational drug use at the start of the pandemic. Controlling for age and race/ethnicity, we tested whether trajectories differed by sex and early-pandemic depressive symptoms, loneliness, and social support.

**Results:** Group-based trajectory models yielded two trajectory groups for binge drinking (none vs. any), marijuana (none/infrequent vs. daily), and recreational drug use (none vs. any). Binge drinking and recreational drug use decreased at the beginning of the pandemic. Generalized linear mixed model supported these trends. Male sex and having depressive symptoms early in the pandemic were positively associated with all three substance use outcomes. Social support was inversely associated with recreational drug use.

**Conclusions:** Contrary to hypotheses, problematic substance use behaviors decreased from pre-pandemic to the post-pandemic follow-up in our sample of PLHIV. Ongoing surveillance is needed to assess whether this pattern persists as the pandemic continues.
ADCC-mediating non-neutralizing antibodies can exert immune pressure in early HIV-1 infection

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Background: Since the RV144 HIV-1 vaccine efficacy trial found that antibody-dependent cellular cytotoxicity (ADCC) responses correlated with lower risk of infection, significant efforts have gone into trying to understand how non-neutralizing antibodies were able to provide protection from infection. An established approach to ascertain the relevance of immune responses is through elucidation of pressure exerted on the virus. A major challenge in characterizing ADCC (antibody-dependent cellular cytotoxicity)-mediated immune pressure in natural infection is that it is difficult to deconvolute Fc-mediated ADCC function from Fab-dependent neutralization function once neutralizing antibodies have developed.

Methods: Here, in five women recruited very early in HIV-1 infection, we determined the timing of detection of neutralizing and ADCC-mediating antibody responses. We then used Sanger single genome and Illumina Miseq sequencing to investigate the kinetics of envelope evolution in early infection and whether escape was detectable before neutralizing antibodies. We then generated pseudoviruses and infectious molecular clones incorporating any mutations observed into the relevant transmitted/founder viruses and conducted functional assays to determine their impact on early neutralizing and ADCC-mediating antibody responses.

Results: We detected low frequency mutations in one participant which escaped ADCC antibody responses but had no effect on neutralizing antibody responses, providing evidence of HIV-1 escape from ADCC responses in early infection for the first time. In comparison, in all participants once neutralizing antibodies were detectable, escape was rapid and occurred at very low titers. Over time, this was the preferred pathway of viral evolution as ADCC sensitive viruses were found to persist, suggesting that nAb had greater impact than ADCC in controlling viral populations.

Conclusions: Overall, this study suggests that if ADCC is playing a role in the protection as shown in human and animal studies, it is likely to occur very early at the foci of infection and the limited immune pressure on the virus suggests that it plays a minor role once infection is established. We believe this finding provides important insights into the role of ADCC and makes a significant contribution to informing HIV vaccine design.
An Adolescent Transition Package (ATP) improves youth readiness to transition to independent HIV care: A cluster randomized trial

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Background: Introduction Transitioning adolescents from pediatric/adolescent to adult care is a critical step in the HIV care continuum. Tools to support transition in sub-Saharan Africa are lacking.

Methods: In a user-centered design, we developed an adolescent transition package (ATP) to provide youth living with HIV (YLH; ages 15-24) with knowledge/skills to transition to independent care. This included serial assessments and chapter-books to systematically guide discussion at clinic visits. Effectiveness of ATP to improve transition readiness was assessed in a cluster randomized controlled trial (NCT03574129). Twenty clinics in 4 counties in Kenya were randomized to ATP or control. Transition readiness was measured using a readiness score comprised of 4 domains (HIV literacy, self-management, communication, support). Readiness scores overall and by domain were compared between arms using mixed-effects linear regression models.

Results: Of 1083 YLH, 587 (54%) were in intervention and 496 (46%) in control sites. Baseline readiness scores differed in ATP and control sites (mean score 12 [SD:3.4] and 11 [SD:3.7], respectively). At year 1, adjusting for baseline scores, participants in the ATP arm had significantly higher overall readiness scores (mean score 16 [SD:1.8] versus 14 [SD:3.3] p=0.01), higher scores in HIV literacy (mean score 4.0 [SD:0.9] versus 3.0 [SD:1.5] p<0.01), self-management (mean score 4.7 [SD:0.4] versus 4.4 [SD:0.6] p=0.015) and communication domains (mean score 4.6 [SD:0.6] versus 4.3 [SD:0.8] p=0.014), respectively.

Conclusions: The ATP significantly improved transition readiness among YLH, increasing literacy, self-management and communication skills. Integrating ATP approaches could enhance long-term HIV care in YLH as they age into adulthood.
Association of cannabinoid with biomarkers of inflammation in persons with HIV

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**Background:** Cannabis use is common among persons with HIV (PWH), but it is unclear whether its use is associated with elevated inflammation – a marker of disease progression among PWH. Prior studies have relied on self-report measurement of cannabis use which can be biased and unreliable. The current study measured cannabis metabolites and markers of inflammation in serum samples of PWH.

**Methods:** Data came from 108 men with HIV who have sex with men. Cannabis metabolites (i.e., 11-nor-9-carboxyTHC (THC-COOH) and biomarkers of inflammation were measured in serum samples. Subjects were classified as heavy and moderate cannabis users if their THC-COOH levels were ≥70 μg/L and <69.9 μg/L, respectively; subjects with undetectable THC-COOH were classified as non-users. We used linear regression models to assess the association between cannabinoid levels and markers of inflammation adjusting for age, methamphetamine use and HIV viral load level.

**Results:** Mean age of the sample was 33 (SD=6.1). Cannabis use was classified as heavy and moderate in 21 (19%) and 40 (37%) participants, respectively, with 47 non-users (40%); 26% had a positive toxicology screen for methamphetamine. Compared to non-users (reference), heavy cannabis use was not significantly associated with any of the inflammatory biomarkers, including high sensitivity C reactive protein (β= −0.20; 95% confidence interval [CI]: −0.88, 0.48), interleukin-6 (β= 0.10; 95% CI: −0.31, 0.51) and tumor necrosis factor-α (β= −0.07; 95% CI: −0.21, 0.08).

**Conclusions:** In this preliminary study, we found no statistically significant association between serum cannabinoids and markers of inflammation. Additional studies using larger samples from longitudinal studies are needed.
A Rapid Enzymatic Assay for Selective Detection of HIV Drugs That Indicate Long-Term and Short-Term PrEP Adherence

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**Background:** Tenofovir diphosphate (TFV-DP) and emtricitabine triphosphate (FTC-TP) are HIV drugs used in PrEP that indicate long-term (1-3 month) and short-term (1-week) medication adherence, respectively. We recently developed the REverSe TRanscrIptase Chain Termination (RESTRICT) assay for rapid measurement of nucleotide analogs based on their inhibition of DNA synthesis by HIV reverse transcriptase (RT) enzyme and demonstrated proof of concept TFV-DP measurement in clinical samples. Here we design RESTRICT assays for selective measurement of both TFV-DP and FTC-TP by accounting for the chemical structure of each drug.

**Methods:** RESTRICT assays were completed by incubating RT, nucleotides, DNA templates, and primers at 37˚C for 30 min followed by addition of PicoGreen® dye to provide fluorescence output. We designed a guanosine-rich DNA template for selective detection of FTC-TP (a deoxycytidine analog) by Watson-Crick-Franklin base pairing and excluded thymidine bases to prevent TFV-DP (a deoxyadenosine analog) binding. Similarly, we designed a thymidine-rich DNA template (excluding guanosine bases) for selective TFV-DP detection. We spiked 1 μM of TFV-DP and FTC-TP into RESTRICT assays with each DNA template and measured endpoint fluorescence. We normalized fluorescence output using “no-enzyme” negative controls and “no drug” positive controls.

**Results:** “No enzyme” controls produced no fluorescence since DNA synthesis did not occur, while “no drug” controls produced maximum fluorescence since there was uninhibited DNA synthesis. RESTRICT assays with guanosine-rich DNA templates produced low fluorescence (4.0 ± 4.3%) with FTC-TP and high fluorescence (86.2 ± 26.3%) with TFV-DP indicating selective FTC-TP detection without cross-reactivity with TFV-DP (p = 0.0060). Conversely, thymidine-rich DNA templates produced high fluorescence (105.7 ± 3.1%) with FTC-TP and low fluorescence (2.4 ± 1.5%) with TFV-DP indicating selective TFV-DP detection (p < 0.0001).

**Conclusions:** The RESTRICT assay enables rapid and selective detection of TFV-DP and FTC-TP. RESTRICT could help to monitor PrEP adherence in near-patient settings (e.g., a doctor’s office or patient’s home) and support treatment monitoring and optimization among special populations like children, pregnant women, and the elderly.
Pandemic Expertise: Findings on the experiences of living with HIV in the COVID-19 pandemic

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Background: People living with HIV (PLWH) generally have increased rates of mental health concerns, unstable housing, food insecurity and substance use than the general population. This baseline vulnerability may leave PLWH particularly susceptible to disruptions resulting from COVID-19 restrictions. In this qualitative study we explored day-to-day experiences of COVID-19 and the public health restrictions among PLWH.

Methods: Patients were recruited from San Francisco General Hospital’s Ward 86 HIV Clinic for either an in-person (n=5) or telephone (n=25) semi-structured interview conducted in English or Spanish. Interviews were audio recorded and transcribed verbatim and translated when necessary. Transcripts were thematically analyzed.

Results: Thirty interviews were conducted August 2020-March 2021 with individuals aged 29-68 years old. The majority were cisgender males (n=21); 6 cisgender women, two transgender women and one transgender man were also interviewed. We identified ‘pandemic expertise’ whereby skills and attitudes developed through the experience of living with HIV helped some PLWH cope with the COVID-19 pandemic, including effective strategies for dealing with anxiety and depression; an appreciation for life; and practical experience of changing behavior to protect their health as a recurring theme. A subset of participants did not share this experience and did not feel that living with HIV helped them to adapt to the COVID-19 pandemic, some perceiving their present lives as chaotic due to lack of stable housing and/or ongoing substance use, without strong personal agency to overcome major challenges. Overall, interviewees reported finding trustworthy health information that helped them understand and adhere to COVID-19 prevention strategies.

Conclusions: This qualitative study in a municipal HIV clinic revealed that, although living with HIV is associated with a higher prevalence of mental health concerns, substance use, and stigma at baseline, these challenges can also contribute to increased self-efficacy, behavioral adaptation, and resilience to face difficult experiences such as the COVID-19 pandemic. Some PLWH may be in a position to share transferrable pandemic skills with fellow patients, such as promoting COVID-19 prevention strategies including vaccination. Stable housing, however, appeared to be key in managing successful adaptation to new adverse experiences and will be needed to respond aggressively to both pandemics.
Sleep Quality is Associated with PrEP Adherence among Young Black Sexual Minority Men

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Background: PrEP adherence among young Black sexual minority men (YBSMM) has been sub-optimal. Sleep has not been explored with regard to PrEP among YBSMM.

Methods: Data were collected from YBSMM in the N2 Cohort Study (N=226). Bivariate and multivariable regression analyses were used to estimate associations between sleep quality and PrEP adherence.

Results: YBSMM who reported sleep disturbance a moderate amount of time (aOR 2.04 [1.04 to 4.02]), (aOR 2.02 [1.02 to 3.98]) or all the time (2.94 [1.05 to 8.20]), (aOR 4.28 [1.47 to 12.49]) were more likely to miss taking PrEP because they forgot, or slept through their dose, respectively.

Conclusions: Sleep quality may negatively impact YBSMM’s ability to consistently take PrEP.
Sex-specific misperceived social norms as drivers of recent HIV testing behavior: a population-based network study of adults in rural Uganda

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**Background:** HIV testing rates have not yet reached the "95-95-95" targets in many HIV-endemic contexts, especially for single adults and for men. Misperceptions about sex-specific recent HIV testing norms as potential drivers of personal testing behavior remain understudied.

**Methods:** Data were collected in 2016-2018 via a network study of all adults within 8 villages in southwest Uganda. Participants reported whether they had tested for HIV within the past 12 months. They also reported whether they thought >50% of men in one’s village and >50% of women in one’s village had done so. The number of adults who were both directly connected to a participant and recently tested per their self-report was also recorded. Multivariable Poisson regression models stratified by marital status and sex were fit to assess the association between personal testing and perceived HIV testing norms.

**Results:** Among 1,624 participants (>91% response rate), most men and most women in every village had been recently tested for HIV. (Sex-specific prevalences ranged from 52-76%.) Additionally, participants had a median of 5 direct connections to others who had been tested recently (IQR: 3-7), and, for 1,316 (81%) participants, at least half of their direct connections had been recently tested. However, only 7% of adults believed that most men had been recently tested, and only 18% of adults believed most women had been recently tested. Single men who misperceived the norm among men were 4.2 times (95% CI 1.2-14.4; P=0.024) more likely to not have been recently tested for HIV compared to single men who thought most men had been tested, adjusting for connections to others who had been tested, knowing an HIV+ person, and other factors. Married women who misperceived the norm among women were also more likely to not have been tested.

**Conclusions:** Most adults mistakenly believed recent testing was not common for either sex in their own village despite it being common in one’s social network and village. These misperceptions were associated with recent HIV testing for single men and married women. Disseminating accurate information about sex-specific HIV testing norms may be a novel way to increase uptake of yearly HIV testing.
Comparing Perspectives of Individuals and HIV Service Providers in response to Health Department HIV Surveillance-Based

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**Background:** The DC Department of Health (HD) conducts multiple surveillance-based interventions (SBI) designed to target individual-level services for those living with or at-risk for HIV. Given the history of stigmatization, discrimination, and racial/ethnic inequity associated with HIV in the U.S., the potential benefits of SBI strategies must be juxtaposed with concerns regarding the privacy and autonomy of individuals targeted for HIV-related outreach efforts. This analysis compares the perspectives of individuals and HIV service providers on these SBIs.

**Methods:** The data used for this analysis was collected as formative research for the “The Development of Responsive Health Department HIV Data to Action Strategies through Community Engagement” project through an anonymous survey of Washington Regional Commission on Health and HIV members attending the 11/21/2019 meeting. This dataset includes 10 respondents who self-identified as either an individual (n=4) or a SP (n=6). Responses were analyzed for similarities and differences across the categories: perceptions, relationship, and engagement.

**Results:** When asked their perceptions of SBIs, individuals reported privacy, stigma, lack of information returned to the community while SPs reported a lack of collaboration and transparency from the HD with privacy, confidentiality, and data security as secondary. When asked about the role of the HD in SBIs and its impact on the individual-provider relationship, Individuals again highlighted privacy as their primary concern with mutual respect indicated as a secondary concern. Among SPs, data collection and sharing were the primary roles. SPs also highlighted the need for more communication from the HD to providers and more empathic communications with community. Lastly, both groups were asked how the HD should engage priority populations. Individuals and SPs agreed the need for consistent feedback, open communication, and mutual respect as chief drivers of engagement. Secondary, incentives to encourage participation were suggested. Both SPs and individuals highlighted the need to engage “new” participants instead of the “faithful few”.

**Conclusions:** This analysis shows individuals prioritize privacy, while SPs prioritize communication within the perception and relationship categories. However, both expressed open communication and incentives to encourage community engagement in SBIs. These similarities and differences were considered as the data collection instruments for the overall project were developed.
Impact of antiretroviral therapy on chronic immune activation and LTBI reactivation in NHP model of TB/SIV co-infection model

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Background: The global control of TB is compounded by co-infection with HIV. Those infected with HIV are at high risk of reactivating LTBI. Viral-induced chronic immune activation correlates with LTBI reactivation due to SIV co-infection. We have earlier shown that initiation of combinatorial antiretroviral therapy 4 weeks post-SIV co-infection failed to prevent TB reactivation despite significantly lowering viral burdens and restoring CD4 T cells in the periphery and lung vasculature. Based on these findings, we hypothesized that timing of cART is critical to control immune activation and thus LTBI reactivation.

Methods: Rhesus macaques were infected with a low dose of 10 CFU Mtb CDC1551 via aerosol. The LTBI macaques were then co-infected with 300 TCID50 SIVmac239 via the intravenous route 9 weeks post-TB infection. 4 macaques were initiated on cART at 2 weeks post-SIV (peak viremia) and 5 macaques-initiated cART at 4 weeks post-SIV (chronic phase of SIV). Statistical analysis was performed using an unpaired Student’s t test, 1- or 2-way ANOVA in GraphPad Prism.

Results: We demonstrate that cART administered at peak viremia enhanced the general well-being of the study animals, controlled the viral replication, improved pathology while significantly reducing the immune activation in BAL and blood. However, cART at peak viremia failed to protect from new TB lesions post-SIV and cART, reconstitute the skewed CD4+ T effector memory responses in the lung compartment, and significantly increased cell proliferation and inflammatory CXCR3+ and CCR6+CD4+ T cells in both BAL and whole blood.

Conclusions: This is the first study to examine the impact of timing of cART on LTBI reactivation in a biologically and physiologically relevant nonhuman primate model. Though the earlier initiation of cART in this study failed to rescue from LTBI reactivation, it resulted in decreased mortality, less disease severity and improved survival. While there doesn’t appear to be an impact of the timing of cART on the CD4 counts, HIV suppression results in maintenance of CD8 responses in the primary infection site as well as in extrapulmonary organs. Further studies aiming at concurrent therapies to contain bacterial burden are needed to have an optimum translational intervention.
United States/Mexico border restrictions in the era of SARS-CoV-2 as a structural driver of HIV risk among drug tourism networks

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Background: Drug tourism (DT) from the U.S. to Mexico is linked to increased HIV risk (sharing injection drug paraphernalia) and paying for sex, and has played an important role in HIV transmission in the border region. Since Tijuana sits on a major transit and drug trafficking route, the closure of the U.S.-Mexican border due to SARS-CoV-2 poses structural HIV risk, as it disrupts cross-border mobility and established social networks. This analysis assesses HIV risk within networks of PWID along the U.S.-Mexican border during the pandemic.

Methods: Participants are from La Frontera, a longitudinal study of PWID aged ≥18 from 3 groups: PWID who injected drugs in Tijuana ≤12 months ago but live in San Diego (SD DTs), and non-drug tourist (NDT) PWID, who live in SD county or Tijuana but have never used illicit drugs across the border. Participants are administered a behavioral questionnaire at baseline, an egocentric social network (SN) survey within two weeks later. Samples undergo HIV serology and genotyping (at baseline). We inferred HIV transmission networks based on a genetic distance threshold of 1.5%. Mixed effects modeling was used to assess sharing of injection equipment with network members (alters).

Results: Of 359 PWID to date who completed the SN survey (104 TJ NDT, 31 SD NDT, 224 SD DT), HIV prevalence was 10.5%; of 34 HIV+, 15 were clustered in a molecular HIV transmission network (consisting of 3 clusters; n=10,3,2) that was significantly associated with drug tourism. Odds of sharing injection equipment with an alter were higher with sex/romantic and drug-use alters, and lower with family compared to friends. Sharing was also positively associated with the alter being a DT, the alter living in Mexico, frequent communication with the alter, the participant being in a phylogenetic cluster, homelessness in the past 6 months, and network size. Sharing was negatively associated with having unstable income.

Conclusions: DTs may be critical to engage in HIV risk reduction interventions as they are more likely to be situated in HIV molecular clusters, and because PWID are more likely to share injecting equipment with DTs, despite the intermittent closure of the US-Mexican border during the pandemic.
Altered Pattern of Circulating miRNAs in HIV Lipodystrophy
Perturb Key Adipose Differentiation and Inflammation Pathways

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**Background:** HIV lipodystrophy is the most prevalent form of acquired lipodystrophy. We identified a unique microRNA (miRNA) profile characterizing HIV lipodystrophy and explored the mechanistic implications on adipocyte biology for the associated clinical phenotype.

**Methods:** miRNA profiles were extracted from small extracellular vesicles (sEV) of HIV-infected individuals with and without lipodystrophic changes and individuals without HIV, among whom we had previously shown differential adipose Dicer expression, demonstrating significant reductions in HIV.

**Results:** miR-20a-3p was increased and miR-324-5p and miR-186 reduced in sEV from HIV lipodystrophic individuals. Changes in these miRNAs correlated with adipose Dicer expression and clinical markers of lipodystrophy, including fat redistribution, insulin resistance, and hypertriglyceridemia. Human preadipocytes transfected with mimic miR-20a-3p, anti-miR-324-5p or anti-miR-186 induced consistent changes in Ltbp2, Wisp2, and Nebl expression. Knockdown of Ltbp2 downregulated markers of adipocyte differentiation (Fabp4, Pparg, C/ebpa, Fasn, adiponectin, Glut4, CD36), and Lamin C, and increased expression of genes involved in inflammation (IL1β, IL6, and Ccl20).

**Conclusions:** Our studies suggest a unique miRNA signature related to dysregulation of Dicer in adipose in HIV. Enhanced miR-20a-3p or depletion of miR-186 and miR-324-5p may downregulate Ltbp2 in HIV leading to dysregulation in adipose differentiation and inflammation, which could contribute to acquired HIV lipodystrophy and associated metabolic and inflammatory perturbations.
Bon Sante (Good Health): Factors Influencing PrEP Utilization Among Haitians and Haitian Americans in Miami, FL

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Background: Haitians (born in Haiti) and Haitian Americans (born in the US) who live in Miami, Florida, are severely impacted by HIV. Despite the effectiveness of Pre-exposure prophylaxis (PrEP), it is underutilized by the Black community. Only 1 percent of Black individuals who could benefit from PrEP receive it. This study provides an in-depth understanding of factors influencing PrEP utilization among Haitians and Haitian Americans living in Miami using a qualitative approach.

Methods: After receiving IRB approval, participants were recruited in collaboration with well-established community partners serving Haitian people in Miami. Participants were adult Haitian and Haitian American individuals (n=30). Community stakeholders (medical providers, members of community and government organizations) (n = 15), and community members (n= 15) were interviewed by bilingual English/Haitian Creole speaking research staff using semi-structured guides in their preferred language. Interviews were recorded, transcribed, translated to English (if needed), coded, and analyzed using thematic content analysis in NVivo.

Results: Participant ages ranged from 23 to 71 years old (15 community stakeholders and 15 community members). Major themes identified were: 1) lack of knowledge regarding PrEP (‘I don’t know anything about it.’); 2) stigma regarding HIV (‘It’s rare to have a Haitian hear that someone has HIV and still hang out with them.’). Other themes include the church, radio and TV as sources of information used by the community and interest in prevention of HIV. Additional themes include the need for privacy regarding sexual health, a preference for oral medication over injections, and need for information regarding medication safety.

Conclusions: Lack of PrEP knowledge and stigma regarding HIV likely impact PrEP utilization among Haitians and Haitian Americans. Interventions to increase PrEP knowledge and decrease stigma regarding HIV need to be evaluated to increase PrEP utilization among Haitians and Haitian Americans. In addition, interventions which include churches, the radio and television as avenues for PrEP information and anti-stigma messaging may be helpful to end the HIV epidemic among Haitians and Haitian Americans.
Using Cognitive Interviews to Evaluate the PHQ-9 for Depression Screening among People Living with HIV in Cameroon

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Background: Depression is highly prevalent among people living with HIV (PLWH) and is associated with additional comorbidities, poor treatment adherence and increased transmission risk. The PHQ-9 is a 9-item screening tool originally developed for use in American primary care settings, via self-administration, assessing intensity of depressive symptoms within the previous 2 weeks. Despite broad implementation, it has been minimally evaluated for comprehension and performance in sub-Saharan Africa or among low-literate PLWH.

Methods: We recruited 24 PLWH >18 years, receiving HIV clinical care in Yaounde, Cameroon. A trained interviewer administered the PHQ-9 in French followed by a cognitive interview (CI): a qualitative interviewing technique used to evaluate response errors, tailor measures to new contexts, and improve validity of quantitative instruments. We used analytic memos and matrices to identify patterns in cognitive response processes by demographic characteristics and PHQ-9 item ratings.

Results: Approximately half of respondents were women (54%); half had primary school education or less (46%); and four (17%) had PHQ-9 scores ≥10, indicating positive depression screen. Overall, respondents comprehended most items as intended, with some exceptions due to double-barreled questions (e.g. ‘moving slowly or being restless’) or lacking relevance to their lives (e.g. ‘overeating’). Some respondents interpreted depressive symptoms (e.g. ‘feeling tired or having little energy’) as “laziness”, and did not report these symptoms in the PHQ-9, despite acknowledging fatigue when probed during the CI. Of the four available response categories (‘Not at all’, ‘Several Days’, ‘More than Half the Days’, ‘Nearly Everyday’) respondents sequentially inverted the two middle categories, citing ‘Several Days’ meant “happening repeatedly”. Additionally, mapping symptoms onto available response categories posed difficulties because respondents did not reference the previous 2-week period, instead anchoring to traumatic events of undefined duration (e.g. HIV diagnosis).

Conclusions: We identified problems related to PHQ-9 comprehension, decision, retrieval and response processes. This tool may neglect presence or intensity of depressive symptoms and conflate others related to HIV status. Further, in low-literacy environments, interviewer-administration may introduce social desirability bias. We suggest changes to time anchor prompts, response category labeling and overall wording to capture culturally relevant expressions of depression to better identify depression among PLWH.
Estrogen Receptor Signaling in macrophages suppresses HIV-associated neurotoxic activity

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Background: Macrophages and microglia (M/M) play pivotal roles in the pathogenesis of HIV-associated neurocognitive disorders. The ensuing inflammatory M/M activation causes neuronal damage. Studies utilizing exogenous anti-inflammatory and antioxidants to mitigate disease progression have been unsuccessful; however, targeting endogenous pathways, such as estrogen signaling may be advantageous. 17β-estradiol, the most active form of estrogen, activates estrogen receptor GPER and has been reported to inhibit HIV infection in primary macrophages and peripheral blood mononuclear cells and protect neurons against HIV proteins, gp120 and tat. Therefore, we hypothesize that low 17β-estradiol concentrations may lead to neuroinflammation during HIV infection, in an estrogen receptor dependent manner.

Methods: To understand this, we stimulated or infected macrophages with HIVJAGO in the presence and absence of increasing doses of 17β-estradiol. Conditioned medium was collected at various time points and placed onto rat cortical neuron to assess neuroinflammation.

Results: We found that low doses of 17β-estradiol had increased neuroinflammation and viral replication. Increasing doses of 17β-estradiol suppressed neurotoxin production and viral replication from HIV-infected macrophages in an estrogen receptor dependent manner.

Conclusions: Given these studies, estrogen signaling may reduce oxidative stress and inflammation seen during neuroinflammatory disorders, such as HIV-associated neurocognitive disorders.
Environmental, Interpersonal, and Individual-Level Factors Associated with Atherosclerotic Cardiovascular Disease Risk Among Women Living with HIV and at Risk for HIV enrolled in the MACS/WIHS Combined Cohort Study

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Background: Women living with HIV (WLWH) have a 2-fold higher risk for atherosclerotic cardiovascular disease (ASCVD) compared to those without HIV infection. While HIV infection is considered a risk factor for ASCVD, estimating the impacts of environmental, interpersonal, and individual-level factors on ASCVD risk may help develop effective interventions to reduce disparities in CVD outcomes and associated risk factors among WLWH.

Methods: We examined the associations between environmental (area-level deprivation and healthcare access), interpersonal (social support and HIV-stigma), and individual-level factors (household income, education, perceived stress, depressive symptoms, and HIV-viral load suppression), and 10-year risk for ASCVD among WLWH (n=1398) and women at risk for HIV (WARH) (n=610) enrolled in the MACS/WIHS Combined Cohort Study (MWCCS). Women were included if they attended a MWCCS visit between April 2013 and October 2019, were 30-79 years of age, and had geospatial data available at the block-group level. The ACC/AHA Pooled Cohorts Risk Equation was used to determine 10-year ASCVD risk. Perceived stress and depressive symptoms were assessed for moderating the effect between area-level deprivation, and ASCVD risk.

Results: Most women were Black (64.5%), with an average age of 52 years. Nearly half (47.6%) had a household income of ≤ $12,000/year, and 62.3% had not attended college. The average 10-year risk for ASCVD was 7.3% among WLWH, compared to 8.4% among WARH. In adjusted multivariable analyses, greater area-level deprivation (β=0.17, 95% CI:-0.0201, 0.3669), household income ≤$12,000/year (β=0.29, 95% CI: 0.1488, 0.4334), less internalized HIV-stigma (β=-0.27, 95% CI: -0.4124, -0.1290), and HIV-viral suppression (β=0.28, 95% CI: 0.1407, 0.4200) were associated with increased risk for ASCVD among WLWH, with depression moderating the impact of area-level deprivation on ASCVD risk (R2=0.034, p<.05). Greater area-level deprivation (β=0.38, 95% CI: 0.0488, 0.7162), household income ≤ 12,000 USD/year (β=0.58, 95% CI: 0.3380, 0.8218), and less social support (β=-0.15, 95% CI: -0.2927, -0.0170)remained associated with greater ASCVD risk in adjusted multivariable analysis among WARH (R =0.08, p< .056).

Conclusions: Area-level deprivation and lower household income were associated with increased risk for ASCVD among WLWH and WARH. Socio-behavioral interventions may be useful to alleviate the negative impact of the environment on ASCVD risk.